UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address COMMISSIONER FOR PATENTS
PO Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,913	05/21/2002	Ernest Arenas	0380-P02709USO	3833

110 7590 07/16/2003

DANN, DORFMAN, HERRELL & SKILLMAN
1601 MARKET STREET
SUITE 2400
PHILADELPHIA, PA 19103-2307

EXAMINER
LEFFERS JR, GERALD G

ART UNIT	PAPER NUMBER
1636	16

DATE MAILED: 07/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,913	ARENAS ET AL.	
	Examiner	Art Unit	
	Gerald G Leffers Jr.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,19-21,23-43,48-54 and 58* is/are pending in the application.

4a) Of the above claim(s) *13-15,23-28,33 and 36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,19-21,29-32,34,35 and 37-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt is acknowledged of a preliminary amendment, filed 11/1/01 as Paper No. 7, in which several claims were amended (claims 4, 6-8, 10-11, 19, 23-25, 37-38, 40, 50), a new claim was added (claim 58) and in which several claims were cancelled (16-18, 22, 44-47 and 55-57). Newly added claim 58 has been placed in nonelected Group III. Claims 1-15, 19-21, 23-43, 48-54 and 58 are pending in the instant application.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-12, 19-21 and 32-40) in Paper No. 9 (filed 4/28/03) is acknowledged. The traversal is on the ground(s) that 1) all of the claims feature neuronal stem or progenitor cells over-expressing in the presence of Type 1 astrocyte factors, 2) several of the claims depend from claims in Group I, or have the exact same language, and therefore must have the same special technical feature, 3) the presence of additional methods steps does not eliminate the original special technical feature, and 4) the impropriety of the requirement is underscored by the fact that the claims were not restricted during international stage. This is not found persuasive because of the following reasons.

With regard to the lack of restriction in the international stage, restriction is optional at any time during prosecution. With regard to the special technical feature not being eliminated just because additional methods steps are required, the argument is not persuasive because the examiner indicated in making the rejection that the dopaminergic cells used in those methods comprising additional steps could have been obtained by other methods. Such dopaminergic cells obtained by induction of dopaminergic cell fate in neuronal precurser cells in response to

increasing levels of expression of Nurr1 in the cells was known in the art at the time of applicants' invention as evidenced by U.S. Patent No. 6,284,539. There is no evidence of record that the cells obtained, for example, by the methods of the cited patent would be different from those obtained by the recited methods. Thus, the presence of additional steps is entirely relevant due to the availability of dopaminergic cells produced by overexpression of Nurr1 in neuronal precursors.

It is further noted that claims 33 and 36 were inadvertently included in Group I when they were actually drawn to a cancelled claim that was appropriately not included in Group I. These claims have also been withdrawn from consideration.

The requirement is still deemed proper and is therefore made FINAL.

Claims 13-18, 22-28, 33 and 36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12, 19-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Each of the claims is directed to a method of inducing a dopaminergic cell fate on a neuronal stem cell or progenitor cell comprising expressing Nurr1 above basal levels within the precurser cell and contacting the precurser cell with one or more factors obtainable from a Type 1 astrocyte of the ventral mesencephalon. Thus, a critical element of the claimed invention is the factor obtainable from a Type 1 astrocyte of the ventral mesencephalon.

The instant specification demonstrates an enhanced direction of neuronal precursor cells expressing Nurr1 to a dopaminergic cell fate when cocultured with Type 1 astrocytes obtained from ventral mesencephalon. The only disclosed utility for the factors obtained from the Type 1 astrocytes is the enhancement of dopaminergic cell fate for neuronal precursors expressing Nurr1. The specification does not, however, describe any such factor. In fact, attempts to provide the factor via cultured media obtained from cultures of Type 1 astrocytes or with membrane fragments of Type 1 astrocytes were unsuccessful. Separation experiments with cocultured precursors and Type 1 astrocytes indicate that at least one such factor is secreted from the astrocytes, but that the secreted factor is highly labile (e.g. page 38, lines 12-28 of the instant specification). No basis at all is provided by the instant specification to envision any specific factor obtainable from Type 1 astrocytes that will satisfy the functional limitations of the claims.

The prior art does not offset the deficiencies of the instant specification with regard to describing factors obtainable from Type 1 astrocytes that are capable of inducing dopaminergic cell fate on neuronal precursor cells expressing Nurr1. In fact, this concept appears to be novel in the art.

Given that the claims encompass a potential broad genus of factors of different types (e.g. secreted and non-secreted factors) that are obtainable from Type 1 astrocytes and the lack of description in the prior art or instant specification of such factors, one of skill in the art would not have been able to envision a sufficient number of embodiments of the claimed invention to describe the broadly claimed genus of such factors. Therefore, one of skill in the art would have reasonably concluded applicants weren't in possession of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12, 18-21, 30-32, 34-35 and 37-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 32, and 34 all feature a limitation where Nurr1 is expressed at levels "above basal levels". The term "basal level" of expression for Nurr1 in the neuronal precurser cells of the invention has not been clearly defined in the instant specification. The term is subjective in the absence of a clearly defined meaning provided by the instant specification. It would be remedial to amend the specification to clearly indicate the level of expression that is required in order to satisfy the limitation of "basal" expression of Nurr1.

Claim 1 comprises the limitation of contacting cells with "one or more factors obtainable from a Type 1 astrocyte" for which the metes and bounds are unclear. For example, it is unclear whether the factor is necessarily obtained from a Type 1 astrocyte or whether that it is merely "obtainable" from a Type 1 astrocyte. Further, it is unclear the conditions during which the

factor is "obtainable" (e.g. development, following treatment with particular growth factors, passage in culture, etc.). It would be remedial to amend the claim to read "obtained from".

Claim 32 is vague and indefinite in that the metes and bounds of the phrase "which contact may result in interaction between the Type 1 astrocyte molecules and the neuronal stem or progenitor cell" are unclear. The term "may" makes it unclear as to whether contact must result in "interaction" or not. Also, the metes and bound of the term "interaction" are unclear. Finally, the metes and bounds of "determining interaction between the Type 1 astrocyte molecules and the stem or progenitor cell" are unclear. This appears to be merely a recitation of a desired outcome without any positive action step to accomplish the desired result, making it clear what is actually done to "determine" interaction.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 19-21 are rejected under 35 U.S.C. 102(e) as being anticipated by Bowen et al (U.S. Patent No. 6,284,539; see the entire patent).

Bowen et al teaches a novel method of directing cell fate for precurser cells of the central nervous system, comprising the introduction and expression of gene coding for the nuclear receptor Nurr1 to direct neuronal precursors to a dopaminergic cell fate (e.g. Abstract; Example

4, column 12). Bowen et al teach compositions comprising differentiated neuronal precursors and additional components (e.g. forskolin in Example 4). There is no evidence of record to indicate that the dopaminergic cells obtained by the methods of Bowen et al would be distinguishable by some structural/functional feature from those claimed herein. The methods of the Bowen et al patent and the instant specification both feature the expression of Nurr1 to drive the developmental fate of the neuronal precurser cells. There is no reason or expectation that the cells obtained from the instant methods somehow change the character of the obtained dopaminergic cells as compared to those obtained by Bowen et al.

Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Conclusion

Claims 1-15, 19-21, 23-43, 48-54 and 58 are pending in the instant application. Claims 13-15, 23-28, 33 and 36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald G Leffers Jr.
Examiner
Art Unit 1636

ggl
July 14, 2003